Involvement of N-6 Adenine-Specific DNA Methyltransferase 1 (N6AMT1) in Arsenic Biomethylation and Its Role in Arsenic-Induced Toxicity

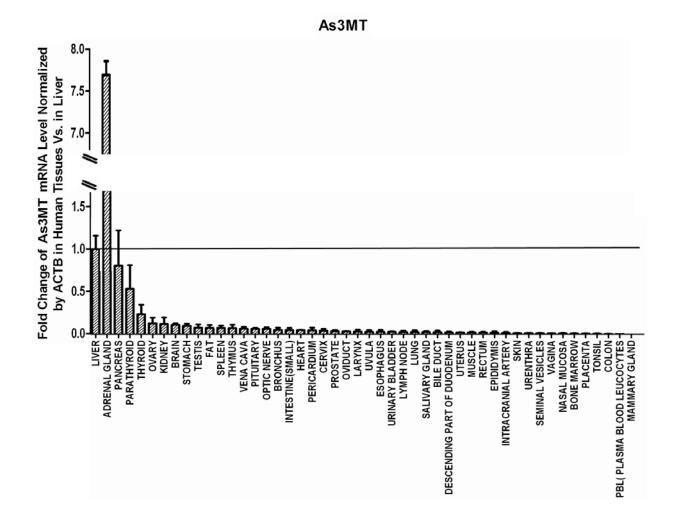
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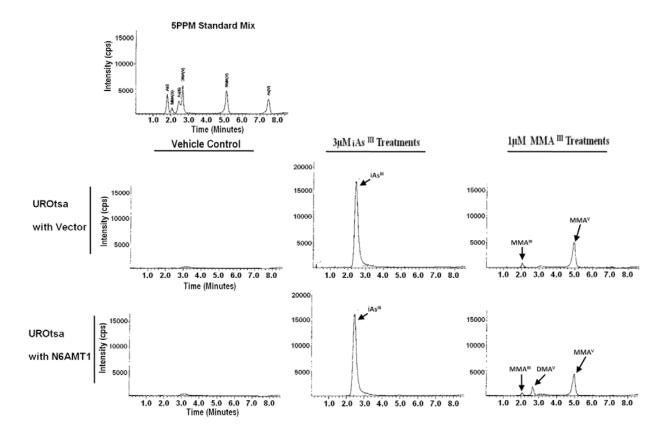
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>gi|87159829| N6AMT1
                          1
                                                    MAGENFATPFHGHVGRGAFSD
                                                                         21
                                                    >gi|109389364| As3MT
                          1 MAALRDAEIQKDVQTYYGQVLKRSADLQTNGCVTTARPVPKHI-REALQN
                                                                         49
>gi|87159829| N6AMT1
                         22 VYEPAEDTFLLLNALEAAAAELA---GVEIC--LEVGSGSGVVSAFLASM
                                                                         66
                                      >gi|109389364| As3MT
                         50 VHEEV-----ALRYYGCGLVIPEHLENCWILDLGSGSGRDCYVLSQL
                                                                         91
>gi|87159829| N6AMT1
                         67 IGPQALYMCTDINP----EAAACTL----E
                            : | . : . . . . . | : . .
                                                       : | : . . | .
>gi|109389364| As3MT
                         92 VGEKGHVTGIDMTKGQVEVAEKYLDYHMEKYGFQASNVTFIHGYIEKLGE
                                Motif II ?
                                                       Motif III ? (D/N)PPY Motif
>gi|87159829| N6AMT1
                         89 TARCNKVHIOPVITDLVKGLLP-----RLTEKVDLLVFNPPYV-V
                            ....|:.| ..|:::.|..|:| |:::....|.|:..|:
>gi|109389364| As3MT
                        142 AGIKNESH-DIVVSNCVINLVPDKQQVLQEAYRVLKHGGELYFSDVYTSL
                                                                         190
>gi|87159829| N6AMT1
                        128 TPPOEVGSHGI------EAAWAGGKNGREVMDRFFPLVPDLLS
                                                                         164
                            ..|:|:.:|.:
                                               1.1.....
>gi|109389364| As3MT
                        191 ELPEEIRTHKVLWGECLGGALYWKELAVLAQKIG-----FCP--PRLVT
                                                                         232
>gi|87159829| N6AMT1
                        165 PKGLFYLVTIKENNPEEIL------KIMKTKGLQ----G
                                                                        193
                               |:||:....|.::
                                                        1...||..|
>gi|109389364| As3MT
                        233 AN----LITIONKELERVIGDCRFVSATFRLFKHSKTGPTKRCQVIYNGG
                                                                         278
>gi|87159829| N6AMT1 194 TTALSR------QAGQETLSVLKFTKS
                                                                         214
                            .1...:
                                             ................
>gi|109389364| As3MT
                        279 ITGHEKELMFDANFTFKEGEIVEVDEETAAILKNSRFAQDFLIRPIGEKL
                                                                         328
>gi|87159829| N6AMT1 215
                                                                      214
>gi|109389364| As3MT 329 PTSGGCSALELKDIITDPFKLAEESDSMKSRCVPDAAGGCCGTKKSC
                                                                      375
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Supplementary Material, Figure 1. Pairwise alignment analysis of N6AMT1 and AS3MT proteins. N6AMT1 and AS3MT proteins share about 25% similarity. Of the three sequence motifs found in most AS3MT homologs, only motif one is highly conserved in N6AMT1. The (D/N) PPY motif present in N6AMT1 is not found in AS3MT.



Supplementary Material, Figure 2. *AS3MT* mRNA expression in human tissues. Expression of *AS3MT* was quantified by rt-qPCR analysis on a panel of 48 normal human tissues, which were normalized by the expression level of *ACTB* and liver was selected as the reference for comparison with all other tissues.



Supplementary Material, Figure 3. Arsenic species profile analysis by HPLC-ICP-MS.

Representative chromatograms of standard control (Upper Image) and samples treated with either iAs^{III} (Lower left panel) or MMA^{III} (Lower right panel) for 3 days between these two cell lines are shown. This figure shows the conversion from MMA^{III} to DMA in URotsa cells with enhanced N6AMT1 expression.